REMARKS

Status of the Claims

Claims 1-24 are pending. Claims 1-4 and 17-24 are canceled due to non-elected claims. Claims 5-16 are rejected. Claims 5, 11 and 12 are amended.

No new matter has been added. Reconsideration of the pending claims is respectfully requested.

Objections to the specification

1. The cross-reference information on the first paragraph of the specification has been amended to update the status of the parent '183 application.

2. Appropriate revision has been made to the "Brief Description of the Drawings" for Figures 4, 12 and 13.

The 35 U.S.C. §112 First Paragraph Rejection

Claims 5-16 are rejected under 35 U.S.C. §112, first paragraph, for lack of enablement. This rejection is respectfully traversed.

The Examiner states that the specification does not enable any person skilled in the art to make and use the invention commensurate in scope with these claims. The Examiner further argues that the failure of the instant specification to give the amount of the DMRIE-C reagent administered causes the instant invention to be unenabled. Applicant respectfully disagree.

Applicant respectfully submits that the Examiner's argument assumes that the DMRIE-C reagent will exert undesirable effects above a certain concentration. However, no ill effects were observed from the topical administration of DMRIE-C in the instant specification. In addition, independent claims 5 and 11 have been amended to recite the wound coverage or closure material is impregnated with a therapeutically effective amount of a cholesterol-containing cationic liposome comprising at least one gene construct encoding a growth factor.

As stated by the Examiner, the as-filed specification provides guidance and working examples about what a therapeutically effective amount of a cholesterol-containing cationic liposome is (see Example 3). Therefore, it is apparent that a skilled artisan could determine without any undue experimentation as to

what is appropriately considered as a therapeutically effective amount of a cholesterol-containing cationic liposome/DNA construct for use within the context of applicant's invention, particularly in view of the totality of the prior art and guidance provided by the as-filed specification. Based on the amendment and arguments given herein, the Applicant asserts that the instant specification enables the application of cationic liposomes for topical gene delivery at external wound sites. Accordingly, Applicant respectfully requests that the rejection of claims 5-16 under 35 U.S.C. §112, first paragraph be withdrawn.

The 35 U.S.C. §103(a) rejections

Claims 5-6, 9, 11-13 are rejected under 35 U.S.C. §103(a) as being obvious by **Goldstein** *et al.* (U.S. Pat. No. 5,962,427) in view of **McDonald** *et al.* (U.S. Pat. No. 6,120,799). This rejection is respectfully traversed.

The instant invention teaches a method of enhancing wound healing of an external wound via direct application of cholesterol-containing cationic liposomes containing DNA encoding growth factors. The claimed methodology improve wound healing

while decreasing the hypermetabolic response which results in lean body tissue loss, acute phase responses such as inflammation, and compromised immune response.

Goldstein *et al.* discloses wound coverage materials incorporating DNA encoding factors that facilitate wound healing. However, as stated by the Examiner, **Goldstein** *et al.* does not teach the use of cholesterol-containing cationic liposomes as a carrier to augment DNA transfection. **McDonald** *et al.* teaches intravenous injection of cationic liposomes containing DNA encoding proteins that stimulate angiogenesis, but does not teach the direct application of cationic liposomes in wounds. Therefore, one of skill in the art would not be motivated to combine the liposomes of **McDonald** *et al.* with the DNA and wound coverage materials of **Goldstein** *et al.* because neither reference provides any evidence that the liposomes will be effective when directly applied to a wound.

In fact, Applicant respectfully submit that **McDonald** *et al.* teaches away from the instant invention in that **McDonald** *et al.* teaches that the liposomes are preferentially taken up by angiogenic endothelial cells in vascular tissues (Column 13, lines 50-54). In contrast, the liposomes of the instant invention were used to efficiently transfect DNA into many different cell types involved in

wound healing including dermal cells, myofibroblasts, endothelial cells, and macrophages. Therefore, based on the combination of **McDonald** *et al.* and **Goldstein** *et al.*, one of skill in the art would assume that, at best, the liposomes would only be effective in delivering DNA to capillary endothelial cells at the wound site. Since **McDonald** *et al.* teaches that cationic liposomes are preferentially absorbed by angiogenic endothelial cells, one of skill in the art would hesitate to use liposomes in a wound site out of fear that the liposomes would direct the majority of the DNA to the capillary endothelial cells and bypass the other cells types to which delivery was also desired. Thus, claims 5-6, 9, 11-13 can not be considered under 35 U.S.C. §103(a) as being obvious over **Goldstein** *et al.* (U.S. Pat. No. 5,962,427) in view of **McDonald** *et al.* (U.S. Pat. No. 6,120,799). Accordingly, Applicant respectfully requests that the rejection of claims 5-6, 9, 11-13 under 35 U.S.C. §103(a) be withdrawn.

Claims 5, 9, 11 and 15 are rejected under 35 U.S.C. §103(a) as being obvious by **Goldstein** *et al.* (U.S. Pat. No. 5,962,427) in view of **McDonald** *et al.* (U.S. Pat. No. 6,120,799),

and further in view of **Coleman** (U.S. 2003/0018984). This rejection is respectfully traversed.

Goldstein *et al.* and **McDonald** *et al.* have been discussed *supra*. **Coleman** et al. teaches gene delivery vectors for controlled expression of recombinant IGF-1 genes within tissues at certain levels (see abstract). Even though **Coleman** *et al.* briefly mentions that IGF-1 encoding expression vector is effective for use to treat an external wound as a result of a nerve crush, **Coleman** *et al.* does not use cholesterol-containing cationic liposomes to deliver the DNA construct. In fact, **Coleman** *et al.* teaches away from the instant invention in that **Coleman** *et al.* teaches that lipids may be useful without forming liposomes (par. 0264, page 23). Therefore, **Coleman** *et al.* provides no teachings that overcome the deficiencies of **Goldstein** *et al.* and **McDonald** *et al.* in rendering obvious the instant invention. Accordingly, Applicant respectfully requests that the rejection of claims 5, 9, 11 and 15 under 35 U.S.C. §103(a) be withdrawn.

Claims 5-8, 11-14 are rejected under 35 U.S.C. §103(a) as being obvious by **Goldstein** *et al.* (U.S. Pat. No. 5,962,427) in view of **McDonald** *et al.* (U.S. Pat. No. 6,120,799), and further in view of

any one of **Baur** (U.S. Pat. No. 4,361,552), **Boyce** (U.S. Pat. No. 5,976,878), **Kushner** (U.S. Pat. No. 5,741,509), and applicant's statement over the prior art on page 29 of the specification. This rejection is respectfully traversed.

Goldstein *et al.* and **McDonald** *et al.* are discussed *supra*. In addition, neither **Goldstein** *et al.* nor **McDonald** *et al.* teach explicitly the types of wound dressings or closure materials as recited in Applicants' claims. Furthermore, none of **Baur, Boyce**, or **Kushner** *et al.* teach the use of cholesterol-containing cationic liposomes to deliver gene construct encoding growth factor. Since none of **Baur, Boyce**, or **Kushner** *et al.* provides teachings that overcome the deficiencies of **Goldstein** *et al.* and **McDonald** *et al.*, no combination of the above references renders the instant invention obvious. Accordingly, Applicant respectfully requests that the rejection of claims 5-8, 11-14 under 35 U.S.C. §103(a) be withdrawn.

The nonstatutory obviousness-type double patenting rejection

Claims 5-16 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-6 of U.S. Patent No. 6,576,618 B1.

Applicant submits a terminal disclaimer in compliance with 37 CFR 1.321 (c) to overcome the nonstatutory double patenting rejection.

This is intended to be a complete response to the Office Action mailed May 06, 2004. Applicant submits that the pending claims are in condition for allowance. If any issues remain outstanding, the Examiner is respectfully requested to telephone the undersigned attorney of record for immediate resolution.

Respectfully submitted,

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Benjamin Aaron Adler, Ph.D.,J.D.
Registration No. 35,423
Counsel for Applicant

ADLER & ASSOCIATES
8011 Candle Lane
Houston, Texas 77071
(713) 270-5391 (tel.)
(713) 270-5361 (fax)
badler1@houston.rr.com